IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: **Hammer, *et al.***	Confirmation No.: **6019**
Serial No.: **10/777,552**	Group Art Unit: 1618
Filing Date: **February 12, 2004**	Examiner: **Leah H. Schlientz**

For: **Polymersomes Incorporating Highly Emissive Probes**

Mail Stop Appeal-Brief Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 41.37

This brief is being filed in support of Appellant's appeal from the rejections of claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101 dated April 7, 2009. A Notice of Appeal was filed on July 7, 2009.

1. REAL PARTY IN INTEREST

Based on information supplied by Appellants and to the best of the undersigned's knowledge, the real parties in interest in the above-identified patent application are the Trustees of the University of Pennsylvania.

2. RELATED APPEALS AND INTERFERENCES

Based on information supplied by Appellants and to the best of the undersigned's knowledge, there are no other appeals or interferences known to Appellants or Appellants' legal representative, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

3. STATUS OF CLAIMS

Rejected: Claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101

Allowed: None

Withdrawn: Claims 14, 24-31, 43-45, 47-51, 64, 66-69, 76, 77, 80-87, 102-107, 109-117, 119-131, 133-141, 143-153, 155-166, 168-170, and 172-184

Objected to: None

Canceled: Claims 2-9, 11, 53, 54, 56-59, 61, 108, 118, 132, 142, 154, 167, and 171

Appealed: Claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101. A listing of the claims involved in the Appeal are listed in the appendix entitled CLAIMS APPENDIX.

4. STATUS OF AMENDMENTS

The amendment made after Final Rejection was entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The following summary is for the purpose of complying with the provisions of 37 CFR 41.37(c)(1)(v). The subject matter of independent claims is summarized below. The entire disclosure, however, should be reviewed to obtain a complete understanding of the claim language. Two independent claims, claims 1 and 52, are on appeal and their basis in the originally filed specification is summarized in the tables below.

Claim 1 Language	Citation to the Specification
A polymersome comprising:	paragraph 0008 on page 3
(i) a plurality of amphiphilic copolymers comprising amphiphilic block copolymers that comprise at least one hydrophilic polymer bonded to at least one hydrophobic polymer; and	paragraph 0008 on page 3
(ii) at least one visible- or near infrared-emissive agent that is dispersed within the polymersome membrane, where said emissive agent emits light in the 700-1100	paragraph 0008 on page 3 and paragraph 0011 on page 4

nm spectral regime and where said emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light that at a wavelength between 700-1100 nm,	
said compound exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the said moieties individually;	paragraph 0011 on page 4
wherein said emissive agent comprises at least two porphyrin moieties, said porphyrin moieties being linked by a hydrocarbon bridge comprising at least one unsaturated moiety.	original claim 5

Claim 52 Language	Citation to the Specification
A polymersome comprising:	paragraph 0008 on page 3
(i) a membrane comprising a plurality of amphiphilic copolymers comprising amphiphilic block copolymers that comprise at least one hydrophilic polymer bonded to at least one hydrophobic polymer;	paragraph 0008 on page 3
(ii) at least one emissive agent that emits light at a wavelength between 700-1100 where said emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light that at a wavelength between 700-1100 nm,	paragraph 0008 on page 3 and paragraph 0011 on page 4

said compound exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the said moieties individually;	paragraph 0011 on page 4
wherein said emissive agent comprises at least two porphyrin moieties, said porphyrin moieties being linked by a hydrocarbon bridge comprising at least one unsaturated moiety; and	original claim 5
(iii) at least one targeting moiety associated with a surface of the polymersome.	paragraph 0024 spanning pages 7-8

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues on appeal are:

(1) whether claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101 were properly rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,159,445 ("the Klaveness patent") in view of Lee, *et al.*, Biotechnol. And Bioeng., 2001, 73, 135-145 ("the Lee article") and further in view of the Chem. Eur. J. 1995, 1, 645-651 ("the Lin article"); and

(2) whether claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101 were properly rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,123,923 ("the Unger patent") in view of Lee, *et al.*, Biotechnol. And Bioeng., 2001, 73, 135-145 ("the Lee article") and further in view of the Chem. Eur. J. 1995, 1, 645-651 ("the Lin article").

7. ARGUMENT

The present invention concerns polymersomes comprising (i) amphiphilic block copolymers having at least one hydrophilic polymer bonded to at least one hydrophobic polymer; and (ii) at least one emissive agent that is a conjugated compound comprising at least two covalently bound porphyrin moieties, linked by a hydrocarbon bridge comprising at least one unsaturated moiety, and dispersed within the polymersome membrane. These emissive agents emit light in the 700-1100 nm spectral regime and exhibit an integral

emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the said moieties individually. The claimed polymerisomes may contain at least one targeting moiety associated with a surface of the polymersome. Such polymersomes can advantageous be utilized in, among other uses, target-specific and locally-active near infrared (NIR)-emissive probes where they show strong signal and long life.

Alleged Obviousness Based on the Klaveness Patent

Claims 1, 10, 12, 13, 15-23, 32-42, 46, 52, 55, 60, 62, 63, 65, 70-75, 78, 79, and 88-101 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 6,159,445 ("the Klaveness patent") and U.S. Patent No. 6, 123,923 ("the Unger patent") in view of Lee, *et al.*, Biotechnol. And Bioeng., 2001, 73, 135-145 ("the Lee article") and further in view of the Chem. Eur. J. 1995, 1, 645-651 ("the Lin article"). To establish a *prima facie* case of obviousness, there must be some reason, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007). Moreover, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The reason to make the claimed combination, and a reasonable expectation of success, must be found elsewhere than in Applicants disclosure, such as in the prior art, the nature of the problem to be solved, or in the knowledge/understanding of the person of ordinary skill in the art. MPEP § 2143; *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Thus, the applicant's disclosure may not be used as a blueprint from which to construct an obviousness rejection. Furthermore, according to MPEP § 2141.02, "[i]n determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." The instant rejection does not meet these requirements.

The Klaveness patent is alleged to disclose contrast agents that have an absorption and/or emission in the 600 to 1300 nm range. September 3, 2008 Office Action at page 8, referenced on page 3 of the April 7, 2009 Final Rejection. Applicants note, however, that the Klaveness patent lists a laundry list encompassing a large number of compositions to be used in this function. *See*, the Klaveness patent at column 15, line 63 to column 16, line 20. The Klaveness patent expressed no preference for porphyrins and, while porphyrins are mentioned generically, there is no teaching or suggestion for the use two porphyrin moieties

linked by a hydrocarbon bridge having at least one unsaturated moiety much less such a moiety that exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the porphyrin moieties individually.

The Office seeks to provide the missing information by importing the teachings of the Lin article to provide disclosure of the porphyrin moieties of the instant claims. As noted above, the instant composition is advantageous over the disclosures of the art. There is nothing in the Lin article that suggests that the instant porphyrin compositions would be an improvement over the moieties used in the primary references. As noted in the instant specification, the multiporphyrins of the instant claims can exhibit an integral emission oscillator strength that is greater than the sum of the oscillator strengths of the monomers. *See*, the instant specification at paragraph 11 spanning pages 4-5. The Lin article teaches nothing about this enhanced property which might make the multiporphyrins of the instant claims to be attractive for use in the methods of the Unger patent. The Examiner dismissed this argument stating that "the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentabilty." April 7, 2009 Final Rejection at page 6. It is not Applicant's suggestion that discovery of a new property is the basis for patentability. Rather, the argument speaks to the lack of motivation to combine the cited art. Without Applicant's patent application in hand and without its teachings of the special properties of the particular porphyrins, sufficient motivation to make to combination of art proposed by the Examiner is lacking.

The Klaveness patent is also defective in its teaching concerning the instant amphiphilic copolymers that have at least one hydrophilic polymer bonded to at least one hydrophobic polymer. As was the case with the contrast agent, the list of carriers for the contrast agent is quite extensive. *See*, the Klaveness patent at columns 12-14 and 17. Based on the extensive list of possibilities, it would not be obvious for one skilled in the art to select amphiphalic block copolymers (column 17, lines 49-50 of the Klaveness patent) for use as a vehicle to carry the contrast agent. Nor is there any guidance or direction to pick and choose the particular combinations that would allow one to arrive at the claimed invention.

The Office seeks to provide the missing information by importing the teachings of the Lee article for the amphiphilic copolymer. As is the case with the use of the prophyrins of the Lin article, there is not sufficient motivation to select the amphilic copolymer of the Lee article. Indeed, the Examiner's proposed reconstruction of the system described by the Klaveness patent would have *none* of the elements taught by the primary patent-- both the

vessel material and the emissive agent are substituted with different materials. As discussed above, there is not sufficient motivation to select the starting points for the Examiner's reconstruction in the Klaveness patent. Viewed in this light, the extent of the reconstruction necessary to allegedly arrive at any instant claim is simply too extensive to be consistent with obviousness. Such a reconstruction would require Applicant's blueprint as a template.

Applicants submit that it is improper for the Examiner to use the claimed invention as an instruction manual to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Fritch*, 972 F.2d 1260, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). The Office can not use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988). In the present reconstruction, as discussed above, *all* elements of the teachings of the primary reference are replaced. Based on these extensive changes to the disclosure of the Klaveness patent, it seems that use of the cited art to arrive at the instant invention can only be derived at through the use of impermissive hindsight based on Applicant's blueprint. For at least this reason, the rejection is improper.

Alleged Obviousness Based on the Unger Patent

The arguments that the Examiner presents to support the rejection based on the Unger patent mirror those presented in regard to the Klaveness patent. *See*, September 3, 2008 Office Action at pages 8-15 and the April 7, 2009 Final Rejection at page 3. For analogous reasons, the Examiner fails to establish a *prima facie* case of obviousness.

The Unger patent, like the Klaveness patent, generically discloses porphyrins among an extensive list of photoactive agents but provides no teaching or suggestion for the use two porphyrin moieties linked by a hydrocarbon bridge having at least one unsaturated moiety much less such a moiety that exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the porphyrin moieties individually. Synthetic vessel forming material are selected form a large list of possibilities where no preference is stated for this possibility. *See*, column 17, line 10 to column 37, line 19 of the Unger patent. In the Unger patent, like the Klaveness patent, there is no clear teaching of all elements of any claim under examination.

The Examiner seeks to cure these defects by asserting the two additional references used in the rejection based on the Klaveness patent. The Lee article is used to provide a disclosure of amphiphilic diblock copolymer and to assert favorable properties attributed to

these compositions. The Lin article is asserted to teach certain linked porphyrins. In the present reconstruction, however, *all* elements from the teachings of the primary reference are replaced by components from the additionally cited art or selected from an extensive list within the primary patent. While the Examiner (April 7, 2009 Final Rejection at page 5) asserts that "[p]atents are relevant as prior art for all they contain", they also must teach enough to lead one skilled in the art to make the claimed combination. It should be noted that porphyrins are only one of many photoactive agents disclosed by the cited art such that it is unclear why one would necessarily choose a porphyrin as opposed to one of the other options, much less choose porphyrin and then pick a porphyrin from the Lin article. Similarly with the amphiphilic diblock copolymer element, it not clear why one skilled in the art would make the changes required by the Office's reconstruction. Based on the significant picking and choosing coupled with the significant changes required to the teachings of Klaveness and Unger patents, it seems that the instant invention can only be derived at through the use of impermissible hindsight based on Applicant's blueprint. Because hindsight reconstruction must be made only with knowledge available to one skilled in the art at the time of the invention and independent of Applicant's blue print, the rejection should be withdrawn.

Conclusion

For the foregoing reasons, Appellant respectfully requests that each of the obviousness rejections advanced in the Final Rejection dated April 7, 2009, be reversed and withdrawn and that the application move forward toward issuance.

Date: October 6, 2009

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8. CLAIMS APPENDIX

1. A polymersome comprising:

(i) a plurality of amphiphilic copolymers comprising amphiphilic block copolymers that comprise at least one hydrophilic polymer bonded to at least one hydrophobic polymer; and

(ii) at least one visible- or near infrared-emissive agent that is dispersed within the polymersome membrane, where said emissive agent emits light in the 700-1100 nm spectral regime and where said emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light that at a wavelength between 700-1100 nm, said compound exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the said moieties individually; wherein said emissive agent comprises at least two porphyrin moieties, said porphyrin moieties being linked by a hydrocarbon bridge comprising at least one unsaturated moiety.

10. The polymersome of claim 1 where at least one of the emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light at a wavelength between 700-1100 nm, is of an intensity that is greater than a sum of light emitted by either of covalently bound moieties individually.

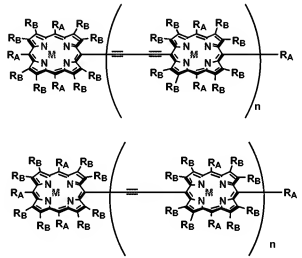
12. A polymersome as in claim 10 where the covalently bound moieties that define the emissive species are linked by at least one carbon-carbon double bond, carbon-carbon triple bond, or a combination thereof.

13. A polymersome as in claim 10 where the covalently bound moieties that define the emissive species are linked by ethynyl, ethenyl, allenyl, butadiynyl, polyvinyl, thiophenyl, furanyl, pyrrolyl, or p-diethylylarenyl linkers or by a conjugated heterocycle that bears diethynyl, di(polyynynyl), divinyl, di(polyvinvyl), or di(thiophenyl) substituents.

15. The polymersome of claim 1 where said polymersome is bioresorbable

16. The polymersome of claim 1 wherein the said emissive agent is an ethynyl- or butadiynyl-bridged multi(porphyrin) compound that features a β-to-β, meso-to-β, or meso-to-meso linkage topology, and the porphinato imaging agent being capable of emitting in the 700-to-1100 nm spectral regime.

17. The polymersome of claim 16 wherein the emissive agent is of the formula:



where M is a metal or H_2, where H_2 denotes the free ligand form of the macrocycle;

R_A and R_B are each, independently, H, C_1-C_{20} alkyl or C_1-C_{20} heteroalkyl, C_6-C_{20} aryl or heteroaryl, $C(R_C)=C(R_D)(R_E)$, $C\equiv C$ (R_D), or a chemical functional group comprising a peptide, nucleoside or saccharide where R_C, R_D and R_E are each independently, H, F, Cl, Br, I, C_1-C_{20} alkyl or C_4-C_{20} heteroalkyl, aryl or heteroaryl, C_2-C_{20} alkenyl or heteroalkenyl, alkynyl or C_2-C_{20} heteroalkynyl, trialkylsilyl, or porphyrinato;

and n is an integer from 1 to 10.

18. The polymersome of claim 17 where n is an integer from 1 to 8.

19. The polymersome of claim 17 where M of the emissive agent is zinc, magnesium, platinum, palladium, or H_2, where H_2 denotes the free ligand form of the macrocycle.

20. The polymersome of claim 17 where said polymersome porphyrin-based imaging agent is emissive.

21. The polymersome of 17, wherein the said emissive agent comprises a meso-to-meso ethyne- or butadiyne-bridged linkage topology, said imaging agent being capable of emitting in the 700-to-1100 nm spectral regime.

22. The polymersome of claim 1 wherein said polymersome comprises one amphiphilic block co-polymer.

23. The polymersome of claim 1 wherein said amphiphilic block co-polymer comprises one hydrophobic polymer and one hydrophilic polymer.

32. The polymersome of claim 1 wherein the amphiphilic co-polymer is made by attaching two strands comprising different monomers.

33. The polymersome of claim 1 wherein the amphiphilic co-polymer comprises polymers made by free radical initiation, anionic polymerization, peptide synthesis, or ribosomal synthesis using transfer RNA.

34. The polymersome of claim 1 wherein the hydrophilic polymer comprises poly(ethylene oxide) or poly(ethylene glycol).

35. The polymersome of claim 1 wherein the hydrophilic polymer is soluble in water.

36. The polymersome of claim 1 wherein the hydrophilic polymer comprises polymerized units selected from ionically polymerizable polar monomers.

37. The polymersome of claim 36 wherein the ionically polymerizable polar monomers comprise an alkyl oxide monomer.

38. The polymersome of claim 37 wherein the alkyl oxide monomer is ethylene oxide, propylene oxide, or any combination thereof.

39. The polymersome of claim 1 wherein the hydrophilic polymer comprises poly(ethylene oxide).

40. The polymersome of claim 1 wherein the volume fraction of the hydrophilic polymers in the plurality of amphiphilic block copolymers is less than or equal to 0.40.

41. The polymersome of claim 1 wherein the hydrophobic polymer comprises polyethylethylene, poly(butadiene), poly(β-benzyl-L-aspartate), poly(lactic acid), poly(propylene oxide), poly(ε-caprolactam), oligo-methacrylate, or polystyrene.

42. The polymersome of claim 1 wherein the hydrophobic polymer comprises polyethylethylene or poly(butadiene).

46. The polymersome of claim 1 wherein the amphiphilic block copolymer is poly(ethylene oxide)-polyethylethylene, poly(ethylene oxide)-poly(butadiene), poly(ethylene oxide)-poly(ε-caprolactone) or poly(ethylene oxide)-poly(lactic acid).

52. A polymersome comprising:

(i) a membrane comprising a plurality of amphiphilic copolymers comprising amphiphilic block copolymers that comprise at least one hydrophilic polymer bonded to at least one hydrophobic polymer;

(ii) at least one emissive agent that emits light at a wavelength between 700-1100 where said emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light that at a wavelength between 700-1100 nm, said compound exhibits an integral emission oscillator strength that is greater than the emission oscillator strength manifest by either one of the said moieties individually; wherein said emissive agent comprises at least two porphyrin moieties, said porphyrin moieties being linked by a hydrocarbon bridge comprising at least one unsaturated moiety; and

(iii) at least one targeting moiety associated with a surface of the polymersome.

55. The polymersome of claim 52 where at least one of the emissive agents has a porphyrin-based component.

60. The polymersome of claim 52 where at least one of the emissive agent is an emissive conjugated compound comprising at least two covalently bound moieties; whereby upon exposing said compound to an energy source for a time and under conditions effective to cause said compound to emit light at a wavelength between 700-1100 nm, is of an intensity that is greater than a sum of light emitted by either of covalently bound moieties individually.

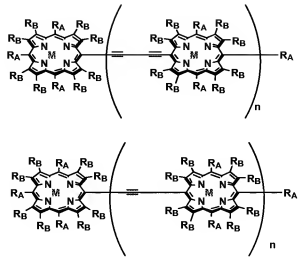
62. A polymersome as in claim 60 where the covalently bound moieties that define the emissive species are linked by at least one carbon-carbon double bond, carbon-carbon triple bond, or a combination thereof.

63. A polymersome as in claim 60 where the covalently bound moieties that define the emissive species are linked by ethynyl, ethenyl, allenyl, butadiynyl, polyvinyl, thiophenyl, furanyl, pyrrolyl, p-diethylylarenyl or any conjugated heterocycle that bears diethynyl, di(polyynynyl), divinyl, di(polyvinvyl), or di(thiophenyl) substituents.

65. The polymersome of claim 52 where said polymersome is bioresorbable.

70. The polymersome of claims 55 wherein the said emissive agent is an ethynyl- or butadiynyl-bridged multi(porphyrin) compound that features a β-to-β, meso-to-β, or meso-to-meso linkage topology, and the porphinato imaging agent being capable of emitting in the 700-to-1100 nm spectral regime.

71. The polymersome of claim 70 wherein the emissive agent is of the formula:



where M is a metal or H_2, where H_2 denotes the free ligand form of the macrocycle;

R_A and R_B are each, independently, H, alkyl or C_1-C_{20} heteroalkyl, C_6-C_{20} aryl or heteroaryl, $C(R_C)=C(R_D)(R_E)$, $C\equiv C(R_D)$, or a chemical functional group comprising a peptide, nucleoside or saccharide where R_C, R_D and R_E are each independently, H, F, Cl, Br, I, C_1-C_{20} alkyl or C_4-C_{20} heteroalkyl, aryl or heteroaryl, C_2-C_{20} alkenyl or heteroalkenyl, alkynyl or C_2-C_{20} heteroalkynyl, trialkylsilyl, or porphyrinato;

and n is an integer from 1 to 10.

72. The polymersome of claim 71 where n is an integer from 1 to 8.

73. The polymersome of claim 72 where M of the emissive agent is zinc, magnesium, platinum, palladium, or H_2, where H_2 denotes the free ligand form of the macrocycle.

74. The polymersome of claim 55 where said polymersome porphyrin-based imaging agent is emissive.

75. The polymersome of 55, wherein the said emissive agent comprises a meso-to-meso ethyne- or butadiyne-bridged linkage topology, said imaging agent being capable of emitting in the 700-to-1100 spectral regime.

78. The polymersome of claim 52 wherein said polymersome comprises one amphiphilic block co-polymer.

79. The polymersome of claim 52 wherein said amphiphilic block co-polymer comprises one hydrophobic polymer and one hydrophilic polymer.

88. The polymersome of claim 52 wherein the amphiphilic co-polymer is made by attaching two strands comprising different monomers.

89. The polymersome of claim 52 wherein the amphiphilic co-polymer comprises polymers made by free radical initiation, anionic polymerization, peptide synthesis, or ribosomal synthesis using transfer RNA.

90. The polymersome of claim 52 wherein the hydrophilic polymer comprises poly(ethylene oxide) or poly(ethylene glycol).

91. The polymersome of claim 52 wherein the hydrophilic polymer is soluble in water.

92. The polymersome of claim 52 wherein the hydrophilic polymer comprises polymerized units selected from ionically polymerizable polar monomers.

93. The polymersome of claim 92 wherein the ionically polymerizable polar monomers comprise an alkyl oxide monomer.

94. The polymersome of claim 93 wherein the alkyl oxide monomer is ethylene oxide, propylene oxide, or any combination thereof.

95. The polymersome of claim 90 wherein the hydrophilic polymer comprises poly(ethylene oxide).

96. The polymersome of claim 95 wherein the volume fraction of the hydrophilic polymers in the plurality of amphiphilic block copolymers is less than or equal to 0.40.

97. The polymersome of claim 52 wherein the hydrophobic polymer comprises polyethylethylene, poly(butadiene), poly(β-benzyl-L-aspartate), poly(lactic acid), poly(propylene oxide), poly(ε-caprolactam), oligo-methacrylate, or polystyrene.

98. The polymersome of claim 97 wherein the hydrophobic polymer comprises polyethylethylene or poly(butadiene).

99. The polymersome of claim 97 wherein the hydrophobic polymer comprises polymerized units selected from ethylenically unsaturated monomers.

100. The polymersome of claim 98 wherein the ethylenically unsaturated monomers are hydrocarbons.

101. The polymersome of claim 52 wherein the amphiphilic block copolymer is poly(ethylene oxide)-polyethylethylene, poly(ethylene oxide)-poly(butadiene), poly(ethylene oxide)-poly(ε-caprolactone) or poly(ethylene oxide)-poly(lactic acid).

9. EVIDENCE APPENDIX

There is no additional evidence provided.

10. RELATED PROCEEDINGS APPENDIX

Applicants are not aware of any related proceedings.